

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-13 (canceled)

Claim 14 (previously amended): A method for producing an antibody combining site in a polypeptide comprising inducing mutagenesis in a complementarity determining region (CDR) of an immunoglobulin light chain gene which comprises amplifying a CDR portion of the immunoglobulin gene by polymerase chain reaction (PCR) using a PCR primer oligonucleotide, said oligonucleotide having 3' and 5' termini and comprising:

a) a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene;

b) a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin gene;

c) a nucleotide sequence between said 3' and 5' termini according to the formula:



wherein N is independently any nucleotide, K is G or T, and n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto;

d) isolating the amplified CDR to form a library of mutagenized immunoglobulin light chain genes;

e) expressing the isolated library of mutagenized light chain genes in combination with one or more heavy chain

genes to form a combinatorial antibody library of expressed heavy and light chain genes; and

f) selecting species of said combinatorial antibody library for the ability to bind a preselected antigen.

Claim 15 (original): The method of claim 14 wherein said 5' terminus has the nucleotide sequence 5'-TATACTGTCAGCAGTAT-3' (SEQ ID NO 26) or 5'-GATTTTGCAGTGTATTACTGTCAGCAGTAT-3' (SEQ ID NO 27), or an oligonucleotide having a sequence complementary thereto.

Claim 16 (original): The method of claim 14 wherein said 3' terminus has the nucleotide sequence 5'-ACTTTCGGCGGAGGGACCAAGGTGGAG-3' (SEQ ID NO 28) or 5'-ACTTTCGGCGGAGGGACC-3' (SEQ ID NO 29), or an oligonucleotide having a sequence complementary thereto.

Claim 17 (original): The method of claim 14 wherein n is 4, 5, 6, 10 or 16.

Claim 18 (original): The method of claim 14 wherein said immunoglobulin is human.

Claim 19 (original): The method of claim 14 wherein said CDR is CDR3.

Claim 20 (original): The method of claim 14 according to the formula: 5'-GATTTTGCAGTGTATTACTGT[NNK]₁₀TTCGGCGGAGGGACCAAGGTGGAG-3' (SEQ ID NO 12), or an oligonucleotide having a sequence complementary thereto.

Claim 21 (previously amended): The method of claim 14 wherein said immunoglobulin light chain gene includes a sequence having the sequence shown in SEQ ID NO 2 or in SEQ ID NO 62.

Claim 22 (previously amended) The method of claim 14 wherein said immunoglobulin light chain gene has the sequence of the light chain gene in ATCC Accession No. 75408.

Claim 23 (canceled)

Claim 24 (previously amended): The method of claim 14 wherein said one or more immunoglobulin heavy chain genes is a library of heavy chain genes.

Claim 25 (previously amended): A method for producing an antibody combining site in a polypeptide comprising inducing mutagenesis in a complementarity determining region (CDR) of an immunoglobulin light chain gene which comprises amplifying a CDR portion of the immunoglobulin gene by polymerase chain reaction (PCR) using a PCR primer oligonucleotide, said oligonucleotide having 3' and 5' termini and comprising:

a) a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene;

b) a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin gene; and

c) a nucleotide sequence between said 3' and 5' termini according to the formula:

$$[MNN]_n,$$

wherein N is independently any nucleotide, M is A or C, n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a

length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto;

d) isolating the amplified CDR to form a library of mutagenized immunoglobulin light chain genes;

e) expressing the isolated library of mutagenized light chain genes in combination with one or more heavy chain genes to form a combinatorial antibody library of expressed heavy and light chain genes; and

f) selecting species of said combinatorial antibody library for the ability to bind a preselected antigen.

Claim 26 (original): The method of claim 25 wherein said 5' terminus has the nucleotide sequence 5'-GTTCCACCTTGGTCCCTTGGCCGAA-3' (SEQ ID NO 30), or an oligonucleotide having a sequence complementary thereto.

Claim 27 (original): The method of claim 25 wherein said 3' terminus has the nucleotide sequence 5'-ACAGTAGTACACTGCAAAATC-3' (SEQ ID NO 31), or an oligonucleotide having a sequence complementary thereto.

Claim 28 (original): The method of claim 25 wherein n is 8, 10 or 16.

Claim 29 (original): The method of claim 25 wherein said immunoglobulin is human.

Claim 30(original): The method of claim 25 wherein said CDR is CDR3.

Claim 31 (previously amended): The method of claim 25 wherein said immunoglobulin light chain gene includes a sequence having the sequence shown in SEQ ID NO 2 or in SEQ ID NO 62.

Claim 32 (previously amended): The method of claim 25 wherein said immunoglobulin light chain gene has the sequence of the light chain gene in ATCC Accession No. 75408.

Claim 33 (canceled)

Claim 34 (previously amended): The method of claim 25 wherein said one or more immunoglobulin heavy chain genes is a library of heavy chain genes.

Claims 35-37 (canceled)